

REMARKS

Applicants wish to thank the Examiner for the careful consideration given to this application. Currently, claims 33-39, 41, 46-62 and 64-77 are pending in this application. Claims 33-39, 41, 47-50, 53, 54, 57, 61, 62, 66, 67, 70, 72, 73, 75 and 76 are currently under consideration. Claims 46, 51, 52, 55, 56, 58-60, 64, 65, 68, 69, 71, 74 and 77 have been withdrawn, and claims 1-32, 40, 42-45 and 63 have been cancelled. Claims 37, 41, 49, 61, 62, 67 and 75 have been amended. No new matter has been added.

35 U.S.C. § 112, second paragraph

Claims 37, 41-43 and 75 stand rejected under 35 U.S.C. § 112, second paragraph, as purportedly being indefinite. Specifically, claims 37, 41 and 75 were rejected for containing terms that lack antecedent basis. Claims 42 and 43 were rejected based on their dependency from claim 41. Applicants have amended claims 37, 41, and 75 to provide appropriate antecedent basis for the identified terms, rendering the Examiner's rejection moot.

35 U.S.C. § 103

The Examiner has rejected claims 33-45, 53-54, 57, 61-63, 66, 67, 70, 72, 73, 75, and 76 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent Publication No. 2004/0096848 to Thru et al. (hereinafter, "Thru"), in view of U.S. Patent No. 5,801,156 to Robinson et al. (hereinafter, "Robinson") and U.S. Patent Publication No. 2004/0259247 to Tuschl et al. (hereinafter, "Tuschl"). Relying heavily on Thru, the Examiner states that "although the reference is directed in particular to LNA, one in the art could use any number of oligomeric compounds of a class of nucleic acid inhibitors as stated in paragraph [0025] which includes siRNA." The Examiner goes on to quote paragraph [0070] of Thru wherein Thru states: "[e]qually well, the LNA oligomeric compounds may be designed as siRNA's which are small double stranded RNA molecules that are used by cells to silence specific endogenous or exogenous genes by an as yet poorly understood "antisense-like" mechanism." Clearly, the Examiner appreciates the limitations of Thru (e.g., directed to a particular LNA and poorly understood "antisense-like" mechanism). What the Examiner fails to appreciate is that Thru's poor understanding of siRNA did not occur until long after Applicant's invention. Rather than support an obviousness rejection, Thru (and its complete lack of appreciation of siRNA as demonstrated by the record) supports patentability of the present claims.

Simply put, Applicant's HIF-1 alpha siRNA claims have a priority date of **October 11, 2002**, and Thrue is not prior art to these claims. In Thrue's U.S. Provisional Application No. 60/370,126, filed April 5, 2002 (hereinafter, the "Thrue Provisional"), Thrue fails to even mention siRNA, and when he does mention siRNA in the non-provisional filed November 4, 2003 he describes it as "poorly understood." Surely the Examiner will not substitute an Examiner's hindsight analysis of Thrue to remedy the clear objective failings of Thrue. Rather than being prior art, Thrue supports the patentability of Applicant's invention.

The subject matter relied upon by the Examiner to reject the present application was not disclosed by Thrue until nearly six months after the priority date of the pending application. Claims 33, 34, 38, 39, 41, 47, 50, 53, 54, 61, 62, 67, 70, 72, 73, 75 and 76 find verbatim support in Applicant's provisional. Although the precise claim language of claims 35-37, 48, 57 and 66 is not recited in Applicant's provisional verbatim, Applicant's attorney respectfully submits that the language of these claims is implicitly described in Applicants' provisional. Although, Applicant's attorney feels it unnecessary, Applicant would consider an Affidavit to antedate Thrue for claims 35-37, 48, 57 and 66.

Neither Robinson nor Tuschl describe methods for inhibiting HIF-1 alpha expression by degrading HIF-1 alpha mRNA, and these references fail to render the claimed methods obvious in the absence of Thrue. Therefore, the combination of Thrue, Robinson and Tuschl fail to render the pending claims obvious and the Examiner's rejection should be withdrawn. Reconsideration is respectfully requested.

Claims 47-50 stand rejected under 35 U.S.C. § 103(a) as being unpatentable of Thrue in view of Robinson and Tuschl, and further in view of Tuschl, et al., *Nature Biotechnology*, Vol. 20:446-448 (2002) (hereinafter, "Tuschl 2002") and U.S. Patent No. 5,624,803 to Noonberg et al. (hereinafter, "Noonberg"). The arguments presented above apply equally well and are incorporated by reference.

As described hereinabove, Thrue fails to predate the pending claims and neither Robinson nor Tuschl teach or suggest methods for inhibiting HIF-1 alpha expression by degrading HIF-1 alpha expression by degrading HIF-1 alpha mRNA. Tuschl 2002 and Noonberg fail to cure these deficiencies. Accordingly, the combination of Thrue, Robinson, Tuschl, Tuschl 2002 and Noonberg fails to render the current claimed invention obvious. Reconsideration and withdrawal of the Examiner's rejection is respectfully requested.

CONCLUSION

In light of the amendments and remarks presented herein, it is believed that the pending claims are in condition for allowance and notice to such effect is respectfully requested. The Commissioner is hereby authorized to charge Deposit Account No. 50-0436 for any additional fees that may be due in connection with this response. Should the Examiner have any questions regarding this application, the Examiner is invited to initiate a telephone conference with the undersigned.

Respectfully submitted,

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